Synthesis of Merocyanine Dyes

Abdu E. ABDEL-RAHMAN* and Zarif H. KHALIL
Chemistry Department, Faculty of Science, Assiut University, Assiut, Egypt, A.R.E.
(Received July 25, 1977)

New 1-ethyl-2-[(2-substituted 3-oxoisoindolin-1-ylidene)methyl]-pyridinium or quinolinium iodide merocyanine dyes were obtained by the reaction of 2-methyl quaternary salts with *N*-substituted phthalimide in the presence of piperidine. 1-Ethyl-2-[(1-substituted 5-oxo-3-pyrrolin-2-ylidene)methyl] quinolinium iodide merocyanines were also prepared. Structural configuration of the synthesised compounds was confirmed by IR and UV spectral determination. 1-Ethyl-2-[[3-oxo-2-(4-phenylthiazol-2-yl)isoindolin-1-ylidene]methyl]-quinolinium iodide has high bactericidal activity againsist *E.Coli*, *Staphylococcus Aureus*, and *Staphylococcus Albas*.

Extensive studies have been made on the preparation and application of merocyanine dyes since their discovery in 1933.[1] In photography, they are widely used as photosensitisers,[2-8] in the production of direct positive photographic emulsions,[9,10] colour films[11-13] electron acceptors,[14] filter dyes,[14,15] and as sensitisers in photoconductive zinc oxide.[16] Phthalimidine dyes of good fastness were patented as dyestuffs for acrylonitrile fibers.[17]

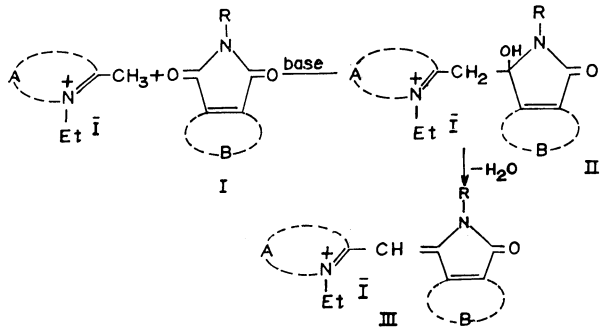
New merocyanine dyes (III-1—22) were prepared. Interaction of 2-methyl quaternary salts with *N*-substituted imides in the presence of piperidine afforded the corresponding compounds (III-1—22) *via* the intermediate (II) which could be separated as colourless needles by the reaction of 1-ethyl-2-methylpyridinium-iodide with *N*-phenylphthalimide. The intermediate (II) is readily soluble in ethanol and in concentrated sulfuric acid from which iodine was liberated on heating. Its IR spectrum revealed an absorption band at 3450 cm^{-1} attributed to –OH group. Dehydration of II to 1-ethyl-2-[(3-oxo-2-phenylisoindolin-1-ylidene)methyl]pyridinium iodide (III-1) was carried out in several ways:

a) Thermal dehydration above melting point.

b) Acid treatment of its ethanolic solution using hydrochloric acid (1 : 1).

c) Prolonged reflux under the reaction conditions and leaving the reaction mixture at room temperature for several days.

The reaction is illustrated as follows:



II. A=Pyridine, R=C_6H_5–, B=C_6H_4–.

III. A=Pyridine, B=C_6H_4–.
1: R=C_6H_5–, 2: R=*p*-CH_3-C_6H_4, 3: R=*p*-CH_3O-C_6H_4, 4: R=*p*-NO_2-C_6H_4, 5: R=*p*-Cl-C_6H_4, 6: R=α-$C_{10}H_7$.

III. A=Quinoline, B=C_6H_4–.
7: R=C_6H_5–, 8: R=*p*-CH_3-C_6H_4, 9: R=*p*-CH_3O-C_6H_4, 10: R=*p*-Cl-C_6H_4, 11: R=*p*-NO_2-C_6H_4, 12: R=*o*-CH_3-C_6H_4, 13: R=*o*-CH_3O-C_6H_4, 14: R=*o*-Cl-C_6H_4, 15: R=α-$C_{10}H_7$, 16: R=β-$C_{10}H_7$, 17: R=CH_2COOH, 18: R=4-phenylthiazol-2-yl.

III. A=Quinoline, B=H.
19: A=*p*-CH_3-C_6H_4, 20: R=*p*-CH_3O-C_6H_4, 21: R=*p*-NO_2-C_6H_4, 22: R=α-$C_{10}H_7$.

Infrared absorption spectra of the newly synthesized compounds showed an absorption band at 1740—1720 cm^{-1} attributed to the carbonyl group >C=O and

TABLE 1. 1-ETHYL-2-[(2-ARYL-3-OXOISOINDOLIN-1-YLIDENE)METHYL]PYRIDINIUM IODIDE MEROCYANINE DYES (III-1—III-6)

Compound No.	Mp °C	Solvent of crystallization	Yield %	Formula	Analysis % Calcd C	H	N	Found C	H	N	Absorption spectra λ_{max} nm(ε)
III-1	178	Dioxane	36	$C_{22}H_{19}N_2OI$	58.15	4.18	6.16	58.20	4.10	6.22	240(57100), 275(37000)
III-2	190—191	Ethanol/H_2O (1 : 1)	38	$C_{23}H_{21}N_2OI$	85.97	4.48	5.98	85.87	4.35	5.78	218(77000), 240(sh)(55200), 325(b.b)(11400)
III-3	145	Ethanol/H_2O (2 : 1)	45	$C_{23}H_{21}N_2O_2I$	57.02	4.34	5.78	57.10	4.38	5.65	215(67800), 245(sh)(35700), 270(28500), 330(25000)
III-4	245	Dioxane	40	$C_{22}H_{18}N_3O_3I$	52.90	3.60	8.41	52.82	3.55	8.25	218(37000), 240(sh)(26000), 310(sh)(17500), 320(20000)
III-5	175	Ethanol/H_2O	28	$C_{22}H_{18}N_2OClI$	54.04	3.68	5.73	54.12	3.70	5.65	220(37700), 240(13900)
III-6	190	Methanol/H_2O	32	$C_{26}H_{21}N_2OI$	61.90	4.16	5.55	62.00	4.12	5.43	215(103000), 285(23400)

(sh)=shoulder, (b.b)=broad band.

Table 2. 1-Ethyl-2-[(2-substituted 3-oxoisoindolin-1-ylidene)methyl]quinolinium iodide merocyanine dyes (III-7—III-18)

Compound	Mp °C	Solvent of crystallization	Yield %	Formula	Analysis % Calcd C	H	N	Found C	H	N	Absorption spectra λ_{max} nm(ε)
III-7	170	D	50	$C_{26}H_{21}N_2OI$	61.90	4.16	5.55	62.00	4.18	5.28	215(155300), 235(sh)(87000), 545(4000), 582(5000)
III-8	178	A	56	$C_{27}H_{23}N_2OI$	62.54	4.44	5.40	62.48	4.40	5.35	215(462000), 240(276000), 540(58000), 584(85000)
III-9	152	A	62	$C_{27}H_{23}N_2O_2I$	60.67	4.30	5.24	60.72	4.25	5.15	215(300000), 238(114000), 548(b.b)(1900), 590(b.b)(2400)
III-10	187	B	48	$C_{26}H_{20}N_2OClI$	57.93	3.71	5.19	57.85	3.80	5.20	213(294000), 243(94000), 520(5800), 557(8900)
III-11	249—250	C	65	$C_{26}H_{20}N_3O_3I$	56.83	3.64	7.65	56.90	3.70	7.58	215(252000), 236(84000), 530(sh)(11700), 556(15600)
III-12	176	A	42	$C_{27}H_{23}N_2OI$	62.54	4.44	5.40	62.60	4.38	5.25	215(133300), 245(45200), 520(sh)(11700), 554(20000)
III-13	141	D	38	$C_{27}H_{23}N_2O_2I$	60.67	4.30	5.24	60.58	4.35	5.19	215(792000), 238(189200), 540(10100), 582(20100)
III-14	128	C	40	$C_{26}H_{20}N_2OCl$	57.93	3.71	5.19	58.15	3.68	4.98	219(441700), 237(509200), 400(b.b)(5500), 490(b.b)(4200), 540(b.b)(4900)
III-15	152—153	B	58	$C_{30}H_{23}N_2OI$	64.98	4.15	5.05	65.10	4.20	5.15	223(64000), 238(b.b)(50000), 450(sh)(18900), 556(38800)
III-16	171	B	65	$C_{30}H_{23}N_2OI$	64.98	4.15	5.05	65.13	4.18	5.18	213(177000), 241(100700), 525(sh)(12500), 560(20830), 604(sh)(8600)
III-17	222—224	D	10	$C_{22}H_{19}N_2OI$	54.32	5.76	5.76	54.27	3.95	5.82	242(71400), 554(12800), 584(15200)
III-18	135	C	32	$C_{29}H_{22}N_3OSI$	59.28	3.74	7.15	59.32	3.70	3.70	242(160000), 540(10570, 586(10000)

A=Ethanol/H_2O(1 : 1), B=methanol, C=dioxane, D=ethanol/H_2O(3 : 1), (sh)=shoulder, (b.b)=broad band.

Table 3. 1-Ethyl-2-[(1-aryl-5-oxo-3-pyrrolin-2-ylidene)methyl]quinolinium iodide merocyanine dyes (III-19—III-22)

Compound No.	Mp °C	Solvent of crystallization	Yield %	Formula	Analysis % Calcd C	H	N	Found C	H	N	Absorption spectra λ_{max} nm(ε)
III-19	124	Ethanol/H_2O (2 : 1)	30	$C_{23}H_{21}N_2OI$	58.97	4.48	5.98	59.05	4.44	6.16	240(10400), 320(4100)
III-20	207	Ethanol/H_2O (1 : 1)	35	$C_{23}H_{21}N_2O_2I$	57.02	4.33	5.78	57.10	4.36	5.58	240(95800), 323(37500)
III-21	205	Dioxane	38	$C_{22}H_{18}N_3O_3I$	62.90	3.61	8.41	62.82	3.58	8.48	——
III-22	242	Methanol/H_2O (1 : 1)	28	$C_{26}H_{21}N_2OI$	61.90	4.16	5.55	62.03	4.20	5.48	221(92000), 238(31000), 280(15500), 320(13700)

another band at 875 cm^{-1} attributed to the terminal double bond on ring –CH=C<. Disappearance of the –NH absorption bands characteristic to the –NH group indicates the disrupture of the *N*-substituted imides.

Absorption spectra of III-1—III-22 showed mainly two or three absorption bands in the UV region; their positions and molar extinction coefficient are dependent on the type of *N*-substituted imides, as well as on that of the quaternary heterocyclic nuclei. The results are given in Tables 1, 2, and 3.

The merocyanine dyes, 1-ethyl-2-[(2-substituted 3-oxoisoindolin-1-ylidene) methyl] quinolinium iodides III-7—III-18 posses mainly two absorption bands in the visible region. Their position and molar extinction coefficient are influenced by the type of *N*-substituents on phthalimide moiety. Thus III-7 possesses two absorption bands at λ_{max} 545 nm, ε_{max} 4000 and another CT band at λ_{max} 582 nm, ε_{max} 5000. Introduction of an electron releasing group to the *p*-position of *N*-phenyl group, causes a red shift which is attributed to the increase of the coplanarity of the molecule (III-8 and III-9).

On the other hand, introduction of an electron withdrawing group to the same position causes a blue shift, (III-10 and III-11). Introduction of the same substituent to the *ortho*- position of *N*-phenyl group causes a blue shift as compared to its *para* isomer (III-8 and III-12; III-10 and III-14), probably due to a hindered rotation of the phenyl ring caused by the *ortho* substituent.

Substitution of the *N*-phenyl moiety with α-naphthyl group causes a blue shift by 26 nm (III-15), whereas the substitution with β-naphthyl group causes a red shift by 22 nm (III-16).

The spectrum of III-18 possesses only one absorption band in the ultraviolet region and two absorption bands in the visible region (Table 3).

Experimental

The IR spectra were determined with a Unicam SP 1200 spectrophotometer using KBr disk wafer technique; absorption spectra in the UV-visible region in ethanol 95% were recorded on a SP 8000 recording spectrophotometer. All melting points are uncorrected.

Preparation of N-*Substituted Phthalimide or Maleimide Derivatives.*[18] A mixture of equimolar proportions of phthalic anhydride (or maleic anhydride) and the amino compound was refluxed in the presence of glacial acetic acid for about 1 h. The product obtained was filtered off and washed with sodium hydrogencarbonate solution, except in the case of glycine when the product was washed with water, then with a few-ml ethanol. The compounds obtained were identical with that reported in litrature, except for the new molecules not reported *e.g. N*-(4-phenylthiazol-2-yl)phthalimide, mp 115—116 °C.

Synthesis of 1-Ethyl-2-[(1-hydroxy-3-oxo-2-phenylisoindolin-1-yl)methyl]pyridinium Iodide (II). Equimolar proportions (0.001 mol) of 1-ethyl-2-methylpyridinium iodide and *N*-phenylphthalimide were dissolved in ethanol (50 ml) to which piperidine (0.5 ml) was added. The mixture was refluxed for 1 h and concentrated to about 15 ml and allowed to cool. Colourless needles precipitated. The product (II) was filtered off, washed with ether and crystallized form aqueous ethanol (1:1) to give colourless needles, mp 156—157 °C. Found: C, 55.62; H, 4.39; N, 5.77, I, 26.5%. Calcd, for $C_{22}H_{21}N_2O_2I$: C, 55.58; H, 4.42; N, 5.89; I, 26.73%

Dehydration of the Intermediate (II). *Thermal Dehydration*: The intermediate was heated at 165—168 °C for 5 min. On colling, orange product was obtained. This was crystallized from dioxane to give orange needles (mp 178 °C).

Acid Treatment: A mixture of II, (0.5 g), ethanol (10 ml) and hydrochloric acid (1 : 1, 10 ml) was allowed to stand for 7 days. Fine orange needles were separated. The product was filtered off, washed with water and few ml of aqueous ethanol (1:1), then crystallized from dioxane to give orange needles, mp with an authentic sample 178 °C.

Prolonged Reflux. A mixture of II (0.5 g), ethanol (10 ml), and piperidine (0.5 ml) was refluxed for 18 h on a water bath. The reaction mixture was concentrated to about 5 ml and allowed to stand at room temperature for 8 days. Orange needles were precipitated. The product (III-1) was collected, washed with ethanol, and crystallized from dioxane to give orange needles, mp and mixed mp 178 °C.

Synthesis of 1-Ethyl-2-[(2-aryl-3-oxoisoindolin-1-ylidene)methyl]pyridinium Iodides, III-1—III-6. A mixture of 1-ethyl-2-methylpyridinium iodide (0.0015 mol), N-arylphthalimide (0.001 mol), ethanol (50 ml), and piperidine (1 ml) was refluxed on a water bath for 14 h. The reaction mixtures were left aside for several days (6—8 day). Coloured crystalline merocyanine dyes III-1—III-6 were deposited. They were filtered off, washed with ether and crystallized from the appropriate solvent. The results are given in Table 1.

Synthesis of 1-Ethyl-2-[(2-substituted 3-oxoisoindolin-1-ylidene)-methyl]quinolinium Iodide Merocyanine Dyes, III-7—III-18. A mixture of 1-ethyl-2-methylquinolinium iodide (0.0012 mol), *N*-substituted phthalimide (0.001 mol), ethanol (50 ml), and piperidine (0.5 ml) was refluxed for 1 h. The mixture was concentrated to about 20 ml and the products were precipitated by addition of water, filtered off, washed with water and then with ether, and crystallized from the appropriate solvent. The results are given in Table 2.

Synthesis of 1-Ethyl-2-[(1-aryl-5-oxo-3-pyrrolin-2-ylidene)-methyl]quinolinium Iodides, III-19—III-22. Equimolar proportions (0.005 mol) of 1-ethyl-2-methylquinolinium iodide, *N*-arylmaleimide, and piperidine (1 ml) in ethanol (50 ml) were refluxed on a water bath for 1 h. The products III-19—III-22 which were precipitated after concentration and dilution with water, were filtered off and crystallized from appropriate solvent. The results are given in Table 3.

Bactericidal Activity of 1-Ethyl-2-[[3-oxo-2-(4-phenylthiazol-2-yl)isoindolin-1-ylidene]methyl]quinolinium Iodide (III-18). The culture medium was normal nutrient agar (NA) medium[19] supplemented with one gram of yeast/litre. The bacterial suspension was prepared by adding one ml of sterile distilled water to a 24 h old culture of the test organism grown on NA slant. One ml aliquots of bacterial suspension were added to Erlenmeyer flasks containing 150 ml of NA and the flasks were incubated for 24 h.

Petri dishes containing sterile modified NA were flooded with the bacterial suspension of the test organisms (2 plates for each organism). Two filter paper discs (one cm diameter) containing merocyanine dye (III-18) dissolved in ethylene glycol (15 mg/l.) were placed on each plate. The plates were incubated at 37 °C for 24 h and the diameter of the inhibition zone was measured. The experiments were repeated 3 times and the results were averaged. Pathogenic bacterial strains *E. Coli*, *Staphylococcus Aureus*, and *Staphylococcus Albas* were supplied by Veterinary Hospital, Ministry of Agriculture, Assiut, Egypt and tested at the Botany Department, Faculty of Science, Assiut University. The results showed remarkable activity towards the tested organisms.

References

1) J. D. Kendal, Brit. Pat., 428222330, Oct. 1933.
2) F. G. Webster and L. G. S. Brooker (Eastman Kodak Co.), U. S. Pat. 3743638, 3 July 1973; Appl. 21210, 19 Mar. 1970.
3) O. Riester (Agfa-Gevaert A.-G.), Ger. Offen., 1916845 (Cl. C O9b. G O3c), 5 Nov. 1970, Appl. 2 Apr. 1969.
4) G. A. Rillaers and H. Depoorter (Agfa-Gevaert A.-G.), Ger. Offen. 1930224 (Cl. C O9b), 15 Jan. 1970. Brit. Appl. 5 July 1968).
5) P. W. Jenkins and L. G. S. Brooker (Eastman Kodak Co.), Fr. Pat. 1573591 (Cl. G O3c), 4 July 1969, U. S. Appl.
6) L. G. S. Brooker, A. Jr. Fumia (Eastman Kodak Co.), Fr. Pat. 1574253 (Cl. G O3c), 11 July 1969, U. S. Appl. 28 July 1967.
7) N. S. Kozlov, O. P. Zhikhareva, and S. A. Batishche, *Khim. Geterotsiki. Soedin.*, **1972**, 1619.
8) G. E. Ficken (Ilford Ltd.), Brit. Pat. 1253468 (Cl. C O9b, G O3c), 17 Nov. 1971, Appl. 3 July 1969.
9) L. L. Lincoln, D. W. Heseltine, (Eastman Kodak Co.) Ger. Offen. 2154124 (Cl. G O3c), 10 May 1972, U. S. Appl. 85707, 30 Oct. 1970.
10) O. Riester, H. Oehalschlanger, and H. Odenwaelder

(Agfa-Gevaert A.-G.), Ger. Offen. 2143967, 8 May 1973, Appl. P.21 42, 967.4, 27 Aug. 1971.
11) E. J. Poppe, Ger. Pat. (East) 71445 (Cl. G O3c), 20 Feb. 1970, Appl. 18 July 1968.
12) K. J. Bannert and D. J. Fry (Slford Ltd.), Brit. Pat. 181020 (Cl. G O3c), 11 Feb. 1970, 4 July 1967.
13) H. Depoorter, Th. H. Ghys (Agfa-Gevaert A.-G.), Ger. Offen., 2106517 (Cl. C O9b), 9 Sep. 1971, Brit Appl. 17 Feb. 1970.
14) E. J. Van Lare (Eastman Kodak Co.), U. S. Pat. 3615608 (Cl. 96/101; G O3c, C O9b), 26 Oct. 1971, Appl. 23 Dec. 1966.
15) F. J. Sauter (Eastman Kodak Co.), Fr. Demande 2190881 (Cl. C O9b. G O3c) 8 Mar. 1974, U. S. Appl. 266028, 26 June 1972.
16) F. G. Webster (Eastman Kodak Co.), Fr. Pat. 1597509 (C l. C O9b, G O3c), 7 Aug. 1970, U. S. Appl. 8 Sept. 1967.
17) H. R. Mueller and M. Seefolder (Badische Anilin-Und Soda-Fabrik A.-G.), Ger. Offen. 1812320 (Cl. C O9b, C O7d), 18 June 1970, Appl. Dec. 1968.
18) A. I. Vogel, "Practical Organic Chemistry," Longmans, Ltd., London (1956), p. 423.
19) E. T. Knudsen and G. N. Rolinson, 1959, Lancet 19/12/59, 1105.